REMARKS/ARGUMENTS

Claims 1, 15-17, 22 and 51-59 are pending. Claims 1, 5 and 59 have been directed to parenteral administration described on page 15, line 7 of the specification. Claim 59 has been limited to treatment of an animal having impaired social activity linked to sexuality. No new matter has been added.

Restriction/Election

The Applicants previously elected Group I, Claims 1-20 and 22, directed to methods for treating a disease using a ligand, and the species of SEQ ID NO: 2 (Gln His Asn Pro Arg) and the species "impaired social activity linked to sexuality". The Restriction Requirement has now been made FINAL.

The original election of species requirement characterizes similar subject matter pertaining to decreased sexuality as being directed to different species. For example, "arousal disorder", "impaired social activity linked to sexuality", and "hypoactive sexual desire disorder" are each indicated as separate species, however, each of these relates to similar phenomena as shown by the experimental data from animal models provided by the specification. Moreover, as shown by the attached review article, Pfaus et al., "What can animal models tell us about human sexual response", sexual excitement, preparatory sexual behaviors, sexual arousal, and copulatory behavior and responses are all identified as appetitive sexual behaviors. Accordingly, the Applicants respectfully request that subject matter pertaining to the effect of administering the QHNPR peptide (SEQ ID NO: 2) for the purpose of increasing or enhancing such sexual responses be examined together.

Objection

Claims 1 and 59 were objected to as generically encompassing nonelected species, that is, species not related to impaired social activity related to sexuality. Since examination may yet be extended to cover additional species, the Applicants will hold their response in abeyance pending the identification of otherwise allowable subject matter. At that time, the non-elected subject matter can be removed, if still required. In the meantime, the generic claims should be examined to the extent they encompass the elected species.

Rejection—35 U.S.C. §112, second paragraph

Claims 15 and 51 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for using the terms "impaired social activity" and "linked to sexuality". The term "impaired social activity linked to sexuality" is defined in the specification page 14, lines 13-16, as an impairment of social relationship to a sexual partner. The Official Action requests an example of impaired social activity linked to sexuality.

As shown by the attached review article, Pfaus et al., "What can animal models tell us about human sexual response", sexual excitement, preparatory sexual behaviors, sexual arousal, and copulatory behavior and responses are all identified as appetitive sexual behaviors which have social components.

Moreover, impaired social activity in rats linked to sexuality is not only well known in the art as shown by Pfaus, but is exemplified by the animal data in the specification by Examples 2-9. Examples 2 to 9 describe a panel of behavior modifications following administration of QHNPR peptide (SEQ ID NO: 2) in rats, e.g. increased interest in environment and capacity for arousal (example 2), increased behavior of the males in the presence of females (example 3), social interaction and interpersonal activities before sexual intercourse (example 4), decreased fear of partner and increased ability to relate (example 5),

loss of avoidance symptoms and enhanced willingness to enter into relationship (example 6) and prolonged social intercourse signs towards female and attention signs to personal toilet (example 7).

Therefore, the Applicants respectfully submit that one with skill in the same field would understand the meaning of "impaired social activity" and "linked to sexuality" and request that this rejection be withdrawn.

Rejection—35 U.S.C. §112, first paragraph

Claims 1, 15-17, 22 and 51-59 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement. The Official Action raises a number of enablement issues which are addressed below:

(1) Route of administration. The claims are now directed to parenteral ("outside the alimentary tract") administration. The specification exemplifies intravenous administration, a form of parenteral administration. Based on the high level of skill in the art, one with skill in the art would have been enabled to select an appropriate route of parenteral administration without undue experimentation. Moreover, such a route of administration would not subject the SMR1 peptide to digestion in the stomach or intestines. Accordingly, the Applicants respectfully request that this ground of rejection be withdrawn.

(2) Relevance of rat model. As shown by the attached review article, Pfaus et al., "What can animal models tell us about human sexual response", humans and other animals, such as rats, share many commonalities with respect to sexual behavior. Tables 1 and 2 in Pfaus depict measures of rodent sexual behavior that can be used to model human sexual behavior (page 11, lines 9 *ff.*). These tables refer to appetitive sexual behavior which includes sexual excitement, preparatory sexual behaviors, sexual arousal, such as penile reflex and noncontact erection, copulatory responses, and copulatory responses.

Furthermore, the use of animal models to model similar human behavior has long been an integral part of medical and scientific research; see the previous Declaration/Affidavit of Dr. Renoncet-Ungeheuer.

Same biochemical mechanism in rats and humans. While the SMR-1 peptide was first identified in rats, as shown in the Declaration of Dr. Rougeot (previously attached) the QHNPR (SEQ ID NO: 2) peptide has the same receptor in rats and in humans: NEP (neutral endopeptidase, also known as neprilysin). NEP is a peptidase that degrades substance P. Substance P is involved in sexual behavior (see the abstract of Argiolas, "Neuropeptides and sexual behavior, previously attached). The QHNPR (SEQ ID NO: 2) peptide inhibits NEP (neprilysin) in rats and humans, see Rougeot et al., PNAS (2003). While the invention is not intended to be limited to a particular mechanism of action, the inhibition of NEP would be expected to reduce the degradation of substance P, thus increasing the levels of substance P available to modulate sexual behavior. In fact, Fig. 1 of the previously attached Declaration of Dr. Rougeot shows just that: that the QHNPR (SEQ ID NO: 2) peptide inhibits the breakdown of substance P by human NEP. These experimental data show that the peptide of SEQ ID NO: 2 is active in humans and regulates molecules such as substance P involved in sexual behavior. Accordingly, one with skill in the art would accept the rat model, and the experimental data of record, as supportive of the effects of SMR1 peptide on the sexual activity of other mammals besides rats.

(3) Normal rats. The Official Action questions the experimental data of record, because so-called normal rats were used in the experiments. However, the Office has not provided any reasoning why the effects of the SMR1 peptide on normal rats would not be predictive of its ability to generally enhance or augment sexual behavior in rats in general. Moreover, "normal rats" are conventionally used to determine the effects of drugs which

enhance various sexual behaviors and sexually-related physiological phenomena, see Pfaus et al.

In addition, the animal models described by Pfaus relate to both male and female animals, see e.g., page 5. While the specification exemplifies enhancement of male social-sexual behavior, the Office has provided no technical or scientific reason (e.g., evidence that females don't produce the SMR1 peptide or lack SMR1 receptors) to doubt that corresponding social-sexual effects would be observed in female animals.

(4) Description of "impaired social activity related to sexuality".

The term "impaired social activity linked to sexuality" is discussed above in regard to the indefiniteness rejection. With respect to enablement, methods of using an SMR1 peptide (e.g., SEQ ID NO: 2) to treat social and sexual dysfunctions in mammals are not only described by the specification, they are extensively exemplified. Such behaviors include increased interest in the environment, capacity for arousal and vocalization (page 18, lines 15-20), increased social and interpersonal activities (page 19, lines 20-22), as well as many other behaviors related to social activity and sexuality described by the data in Examples 2-9. Thus, the specification demonstrates that the SMR1 peptide (SEQ ID NO: 2) improved a panel of sexual/social behaviors in rats and rats are a useful model of these behaviors in other mammals as shown by Pfaus.

For the reasons expressed above, the Applicants respectfully request that this rejection be withdrawn.

Rejections—35 U.S.C. §112, first paragraph

Claims 1, 15-17, 22 and 51-59 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate description.

The Official Action indicated that the specification does not disclose the treatment of humans. The Applicants respectfully traverse this ground of rejection, because original Claim 1 refers to treatment of mammals and page 7, lines 16-17, of the specification describe "mammals" as including humans. While treatment of humans is not exemplified in the disclosure, exemplification is not required for adequate description. Therefore, the original disclosure contemplates and discloses the treatment of mental diseases in humans using SMR1 peptides. The elected species to which examination is presently directed (impaired social activity linked to sexuality) is disclosed by page 16, line 26 of the specification and by Claim 15. Page 15, lines 5-15 and Claim 22 describe various routes of administration as well as dosages of the SMR1 peptides. Therefore, all of the claimed subject matter is described by the original disclosure.

The Official Action indicates that the point of this description rejection was that "applicants were not in possession of a method of treating any mental disorder or sexual disorder in humans or animals" and were not in possession of the routes of administration for the SMR-1 peptide. However, as pointed out above, all the claimed subject matter finds descriptive support in the specification.

The Examiner's concern appears to be whether or not the invention was enabled as of its filing date and not whether the Applicants described the claimed invention. Accordingly, the Applicants respectfully submit that this description rejection be withdrawn and the Examiner's concerns with regard to whether the invention is enabled merged into the enablement rejection which is addressed above.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application as directed to the elected species is now in condition for allowance. Thus, extension of examination to additional species and subsequent allowance of this application is earnestly requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon

Thomas M. Cunningham
Registration No. 45,394

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 06/04)
NFO/TMC:aif